Developing gene therapy for dominant optic atrophy using human pluripotent stem cell-derived retinal organoid disease models

Grant Award Details

Developing gene therapy for dominant optic atrophy using human pluripotent stem cell-derived retinal organoid disease models

Grant Type: Quest - Discovery Stage Research Projects

Grant Number: DISC2-13475

Investigator:

Name:	Xian-Jie Yang
Institution:	University of California, Los Angeles
Type:	PI

Award Value: $1,345,691

Status: Pre-Active

Grant Application Details

Application Title: Developing gene therapy for dominant optic atrophy using human pluripotent stem cell-derived retinal organoid disease models

Public Abstract:

Research Objective

We will develop a gene therapy for a major inherited optic nerve disease and test the effectiveness of the treatment by analyzing healthy and patient stem cell-derived mini human retinas.

Impact

The research will use stem cell-based methods to overcome the shortage of human retinal cells and establish disease models, thus allow testing of novel therapeutic treatments for blinding diseases.

Major Proposed Activities

- Using stem cell technology to derive mini human retinas and to identify impaired cellular functions of patient retinal neurons by comparison to healthy human retinal neurons
- Using stem cell-derived mini retinas to determine the capacity of patient retinal neurons to survive under normal and stressed growth conditions
- Using stem cell-derived mini retinas to examine the abnormal levels and forms of the mutant protein produced in patient's retinal cells, thus identifying the key deficiency of the disease
- Using stem cell-derived mini retinas to study the physiological properties of patient's retinal neurons and determine the visual functional deficits
- Producing the gene therapy vehicles for delivering the functional proteins to patient's retinal neurons
- Using stem cell-based mini retinas to test the gene therapy vehicles for their capacity to to transduce retinal neurons and to recuse the disease pathology

Statement of Benefit to California:

This proposed research will yield the first therapeutic candidate for treating dominant optic atrophy. Since the defective mutant gene can also cause Parkinson's disease, the study may facilitate a broader research in neurodegenerative diseases, thus benefiting Californians. The research will strengthen the leading position of California in stem cell technology by circumventing the shortage of human retinal cells and accelerating drug discovery for major blinding diseases including glaucoma.

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